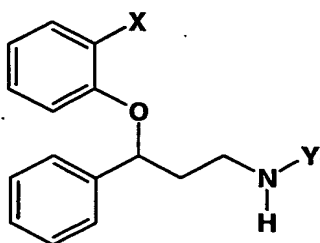


-318-

We Claim:

1. A method of preventing or treating hot flashes, vasomotor symptoms, impulse control disorders, or personality change due to a general medical condition, comprising administering to a patient in need thereof a therapeutically effective amount of a selective norepinephrine reuptake inhibitor selected from the group consisting of:

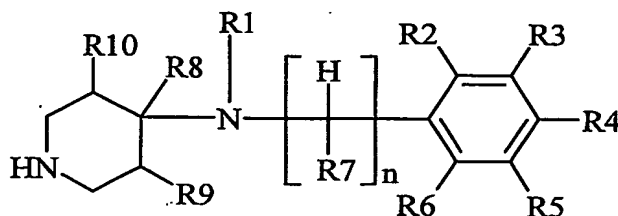
- atomoxetine or a pharmaceutically acceptable salt thereof;
- racemic reboxetine or a pharmaceutically acceptable salt thereof;
- (S,S) reboxetine or a pharmaceutically acceptable salt thereof;
- a compound of formula (I):



(I)

wherein X is C₁-C₄ alkylthio, and Y is C₁-C₂ alkyl, or a pharmaceutically acceptable salt thereof;

a compound of formula (IA):



(IA)

wherein n is 1, 2 or 3; R₁ is C₂-C₁₀alkyl, C₂-C₁₀alkenyl, C₃-C₈cycloalkyl or C₄-C₁₀cycloalkylalkyl, wherein one C-C bond within any cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond and wherein each group is optionally substituted with from 1 to 7 halogen substituents and/or with from 1 to 3 substituents each independently selected from hydroxy, cyano, C₁-C₄alkyl, C₁-C₄alkylthio (optionally substituted with from 1 to 3 halogen atoms) and C₁-C₄alkoxy (optionally substituted

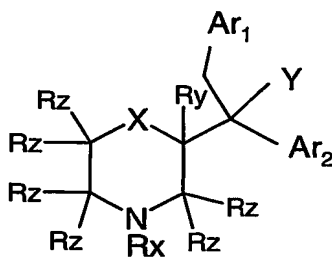
-319-

with from 1 to 3 halogen atoms); R2 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R3 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R2 or R4 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R4 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R5 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R6 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally

-320-

substituted with from 1 to 7 halogen atoms) or halogen; R7 is H or C₁-C₄alkyl; R8 is H or C₁-C₄alkyl; R9 is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; and R10 is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; or a pharmaceutically acceptable salt thereof, with the proviso that the compound N-ethyl-N-benzyl-4-piperidinamine is excluded;

a compound of formula (IB):

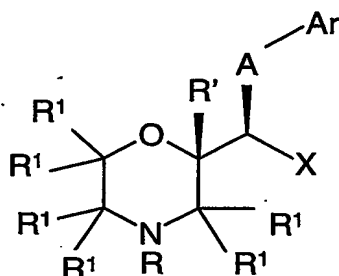


(IB)

wherein R_x is H; R_y is H or C₁-C₄ alkyl; each R_z is independently H or C₁-C₄ alkyl; X represents O; Y represents OH or OR; R is C₁-C₄ alkyl; Ar₁ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl), S(C₁-C₄ alkyl), halo, hydroxy, pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); and Ar₂ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl) and halo; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof;

a compound of formula (IC)

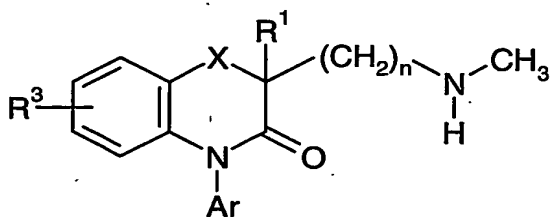
-321-



(IC)

wherein: A is S or O; R is H; Ar is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl), S(C₁-C₄ alkyl), halo, hydroxy, CO₂(C₁-C₄ alkyl), pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); X is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); a C₁-C₄ alkyl group; a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group; R' is H or C₁-C₄ alkyl; each R¹ is independently H or C₁-C₄ alkyl; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof; with the proviso that, when A is O, X is a C₁-C₄ alkyl group, a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group;

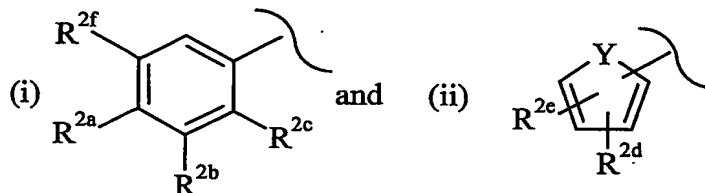
a compound of formula (ID)



(ID)

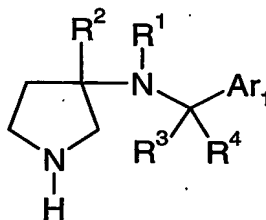
wherein -X- is -C(R⁴R⁵)-, -O- or -S-; n is 2 or 3; R¹ is H or C₁-C₄ alkyl; R³ is H, halo, C₁-C₄ alkyl, O(C₁-C₄ alkyl), nitrile, phenyl or substituted phenyl; R⁴ and R⁵ are each independently selected from H or C₁-C₄ alkyl; Ar- is selected from the group consisting of

-322-



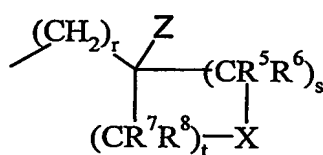
in which R^{2a} is H, halo, methyl or ethyl; R^{2b} is H, halo or methyl; R^{2c} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2d} is H, halo, methyl or ethyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2f} is H, or fluoro; -Y- is -O-, -S- or -N(R^6)-; and R^6 is H or methyl or a pharmaceutically acceptable salt thereof;

a compound of formula (IE)

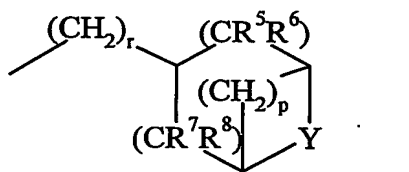


(IE)

wherein R^1 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3 - C_6 cycloalkyl), -SO₂-(C_1 - C_3 alkyl), -CN, -COO-(C_1 - C_2 alkyl) and -OH); C_2 - C_6 alkenyl; -(CH₂)_q-Ar₂; or a group of formula (i) or (ii)



(i)



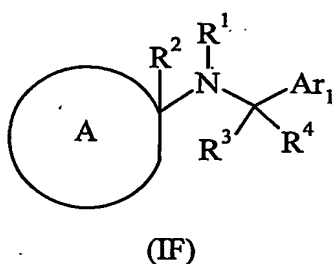
(ii)

R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1 - C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1 - C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C_1 - C_4 alkyl) (optionally

-323-

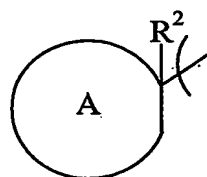
substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents) and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; (d) when -Y- is -O- then p cannot be 0; and (e) the compound 3-[(phenylmethyl)-(3S)-3-pyrrolidinylamino]-propanenitrile is excluded;

a compound of formula (IF)

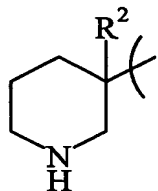


wherein

-324-

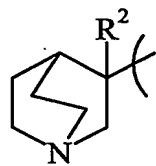


is a group of formula (a) or (b)



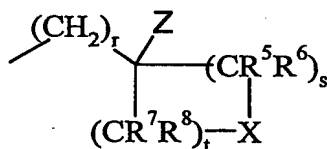
(a)

or

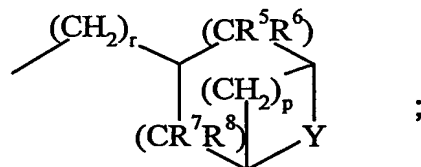


(b)

R^1 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3 - C_6 cycloalkyl), -SO₂-(C_1 - C_3 alkyl), -CN, -COO-(C_1 - C_2 alkyl) and -OH); C_2 - C_6 alkenyl; -(CH₂)_q-Ar₂; or a group of formula (i) or (ii)



(i)



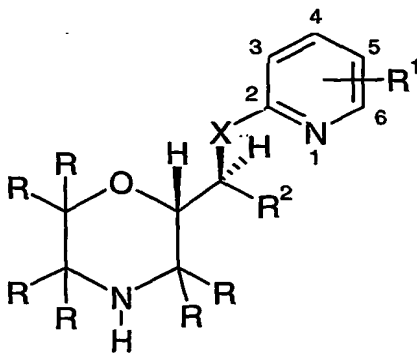
(ii)

R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1 - C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1 - C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents), benzyl and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1 -

-325-

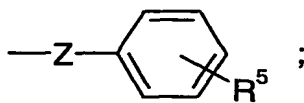
C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; and (d) when -Y- is -O- then p cannot be 0;

a compound of formula (IG)



(IG)

wherein -X- is -S- or -O-; each R is independently selected from H or C₁-C₄ alkyl; R¹ is H, C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, trifluoromethyl, trifluoromethoxy, -NR³R⁴, -CONR³R⁴, -COOR³ or a group of the formula (i)

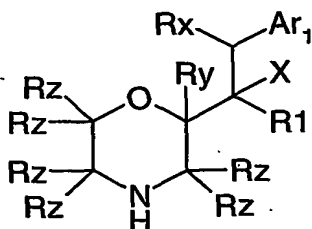


(i)

R² is C₁-C₄ alkyl, phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, -NR⁶R⁷, -CONR⁶R⁷, COOR⁶, -SO₂NR⁶R⁷ and -SO₂R⁶; R⁵ is selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, carboxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, -NR⁸R⁹, -CONR⁸R⁹, -SO₂NR⁸R⁹ and -

-326-

SO_2R^8 ; R^3 , R^4 , R^6 , R^7 , R^8 and R^9 are each independently selected from H or C₁-C₄ alkyl; and -Z- is a bond, -CH₂-, or -O-; or a pharmaceutically acceptable salt thereof and a compound of formula (IH)



(IH)

wherein,

X is OH, C₁-C₄ alkoxy, NH₂ or NH(C₁-C₄ alkyl);

Rx is H or C₁-C₄ alkyl;

Ry is H or C₁-C₄ alkyl;

each Rz group is independently H or C₁-C₄ alkyl, with the proviso that not more than 3 Rz groups may be C₁-C₄ alkyl;

R₁ is C₁-C₆ alkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C₁-C₄ alkylthio (optionally substituted with 1, 2 or 3 fluorine atoms), C₁-C₄ alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms), C₃-C₆ cycloalkoxy, C₁-C₄ alkylsulfonyl, cyano, -CO-O(C₁-C₂ alkyl), -O-CO-(C₁-C₂ alkyl) and hydroxy); C₂-C₆ alkenyl (optionally substituted with 1, 2 or 3 halogen atoms); C₃-C₆ cycloalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C₁-C₄ alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; C₄-C₇ cycloalkylalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C₁-C₄ alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; or CH₂Ar₂; and Ar₁ and Ar₂ are each independently a phenyl ring or a 5- or 6-membered heteroaryl ring each of which is optionally substituted with 1, 2 or 3 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C₁-C₄ alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C₁-C₄ alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C₁-C₄ alkyl), cyano, -NRR, -CONRR, halo and hydroxy

-327-

and/or with 1 substituent selected from pyridyl, thiophenyl, phenyl, benzyl and phenoxy each of which is optionally ring-substituted with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO₂NRR and SO₂R); and
each R is independently H or C1-C4 alkyl;

or a pharmaceutically acceptable salt thereof.

2. Use of a selective norepinephrine reuptake inhibitor for the manufacture of a medicament for the treatment of hot flashes, vasomotor symptoms, impulse control disorders, or personality change due to a general medical condition,

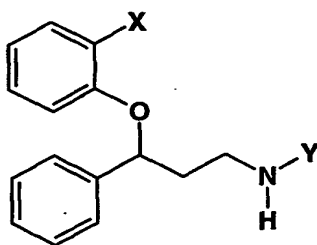
wherein said selective norepinephrine reuptake inhibitor is selected from the group consisting of:

atomoxetine or a pharmaceutically acceptable salt thereof;

racemic reboxetine or a pharmaceutically acceptable salt thereof;

(S,S) reboxetine or a pharmaceutically acceptable salt thereof;

a compound of formula (I):

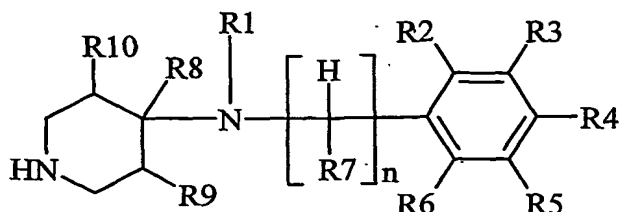


(I)

wherein X is C₁-C₄ alkylthio, and Y is C₁-C₂ alkyl, or a pharmaceutically acceptable salt thereof;

a compound of formula (IA):

-328-



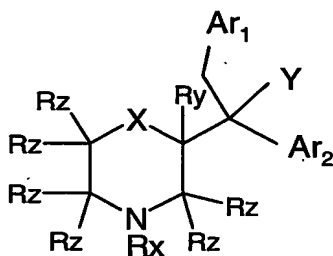
(IA)

wherein n is 1, 2 or 3; R1 is C₂-C₁₀alkyl, C₂-C₁₀alkenyl, C₃-C₈cycloalkyl or C₄-C₁₀cycloalkylalkyl, wherein one C-C bond within any cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond and wherein each group is optionally substituted with from 1 to 7 halogen substituents and/or with from 1 to 3 substituents each independently selected from hydroxy, cyano, C₁-C₄alkyl, C₁-C₄alkylthio (optionally substituted with from 1 to 3 halogen atoms) and C₁-C₄alkoxy (optionally substituted with from 1 to 3 halogen atoms); R2 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R3 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R2 or R4 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R4 is H, C₁-C₄alkyl (optionally substituted

-329-

with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₃ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R₅ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R₆ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R₇ is H or C₁-C₄alkyl; R₈ is H or C₁-C₄alkyl; R₉ is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; and R₁₀ is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; or a pharmaceutically acceptable salt thereof, with the proviso that the compound N-ethyl-N-benzyl-4-piperidinamine is excluded;

a compound of formula (IB):



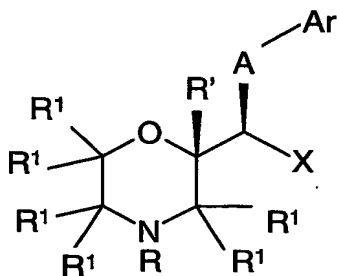
(IB)

wherein R_x is H; R_y is H or C₁-C₄ alkyl; each R_z is independently H or C₁-C₄ alkyl; X represents O; Y represents OH or OR; R is C₁-C₄ alkyl; Ar₁ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl), S(C₁-C₄ alkyl), halo, hydroxy, pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); and Ar₂ is a phenyl ring or a 5- or 6-membered

-330-

heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl) and halo; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof;

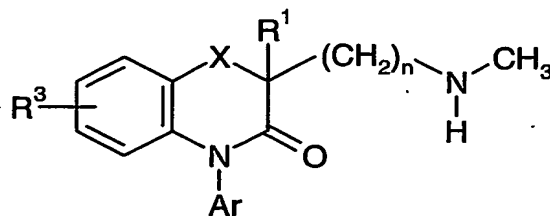
a compound of formula (IC)



(IC)

wherein: A is S or O; R is H; Ar is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl), S(C₁-C₄ alkyl), halo, hydroxy, CO₂(C₁-C₄ alkyl), pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); X is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); a C₁-C₄ alkyl group; a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group; R' is H or C₁-C₄ alkyl; each R¹ is independently H or C₁-C₄ alkyl; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof; with the proviso that, when A is O, X is a C₁-C₄ alkyl group, a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group;

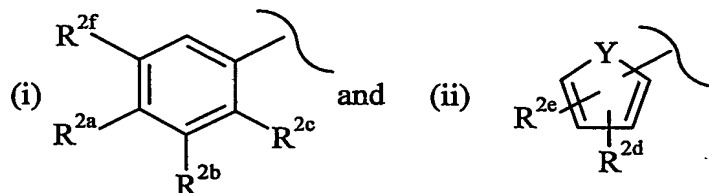
a compound of formula (ID)



(ID)

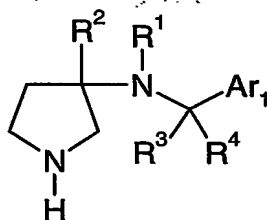
-331-

wherein -X- is $-C(R^4R^5)-$, -O- or -S-; n is 2 or 3; R^1 is H or C_1-C_4 alkyl; R^3 is H, halo, C_1-C_4 alkyl, $O(C_1-C_4$ alkyl), nitrile, phenyl or substituted phenyl; R^4 and R^5 are each independently selected from H or C_1-C_4 alkyl; Ar- is selected from the group consisting of



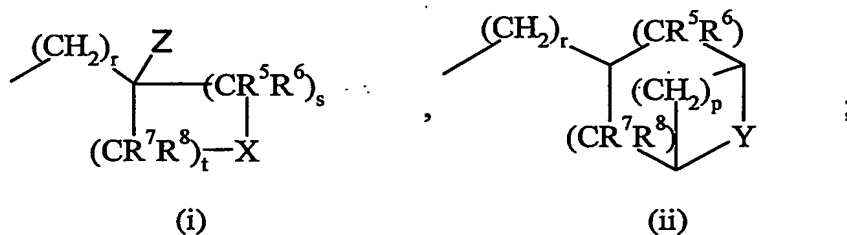
in which R^{2a} is H, halo, methyl or ethyl; R^{2b} is H, halo or methyl; R^{2c} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2d} is H, halo, methyl or ethyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2f} is H, or fluoro; -Y- is -O-, -S- or $-N(R^6)-$; and R^6 is H or methyl or a pharmaceutically acceptable salt thereof;

a compound of formula (IE)



(IE)

wherein R^1 is C_1-C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1-C_3 alkyl), -O-(C_1-C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3-C_6 cycloalkyl), -SO₂-(C_1-C_3 alkyl), -CN, -COO-(C_1-C_2 alkyl) and -OH); C_2-C_6 alkenyl; $-(CH_2)_q-Ar_2$; or a group of formula (i) or (ii)

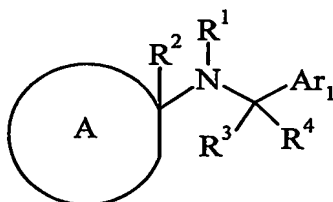


R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1-C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1-C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1-C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or

-332-

thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents) and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; (d) when -Y- is -O- then p cannot be 0; and (e) the compound 3-[(phenylmethyl)-(3S)-3-pyrrolidinylamino]-propanenitrile is excluded;

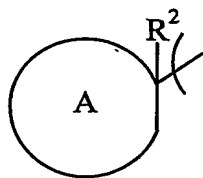
a compound of formula (IF)



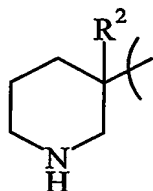
(IF)

wherein

-333-

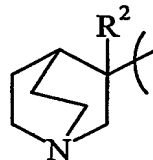


is a group of formula (a) or (b)



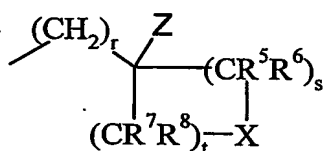
(a)

or

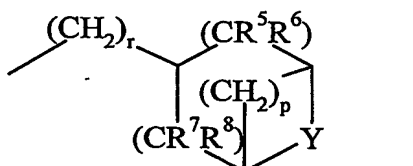


(b)

R¹ is C₁-C₆ alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C₁-C₃ alkyl), -O-(C₁-C₃ alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C₃-C₆ cycloalkyl), -SO₂-(C₁-C₃ alkyl), -CN, -COO-(C₁-C₂ alkyl) and -OH); C₂-C₆ alkenyl; -(CH₂)₄-Ar₂; or a group of formula (i) or (ii)



(i)



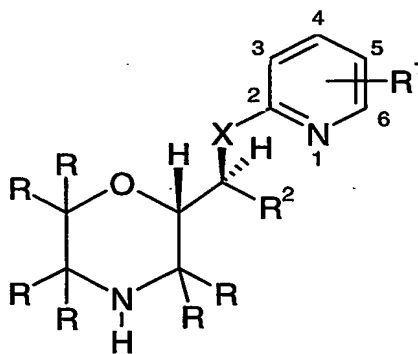
(ii)

R², R³ and R⁴ are each independently selected from hydrogen or C₁-C₂ alkyl; R⁵, R⁶, R⁷ and R⁸ are at each occurrence independently selected from hydrogen or C₁-C₂ alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C₁-C₃ alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents), benzyl and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-

-334-

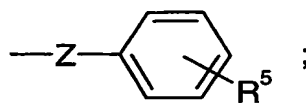
C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; and (d) when -Y- is -O- then p cannot be 0;

a compound of formula (IG)



(IG)

wherein -X- is -S- or -O-; each R is independently selected from H or C₁-C₄ alkyl; R¹ is H, C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, trifluoromethyl, trifluoromethoxy, -NR³R⁴, -CONR³R⁴, -COOR³ or a group of the formula (i)

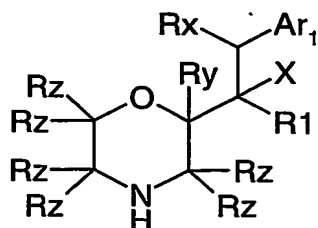


(i)

R² is C₁-C₄ alkyl, phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, -NR⁶R⁷, -CONR⁶R⁷, COOR⁶, -SO₂NR⁶R⁷ and -SO₂R⁶; R⁵ is selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, carboxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, -NR⁸R⁹, -CONR⁸R⁹, -SO₂NR⁸R⁹ and -

-335-

SO_2R^8 ; R^3 , R^4 , R^6 , R^7 , R^8 and R^9 are each independently selected from H or C₁-C₄ alkyl; and
 -Z- is a bond, -CH₂-, or -O-; or a pharmaceutically acceptable salt thereof and
 a compound of formula (IH)



(IH)

wherein,

X is OH, C₁-C₄ alkoxy, NH₂ or NH(C₁-C₄ alkyl);

Rx is H or C₁-C₄ alkyl;

Ry is H or C₁-C₄ alkyl;

each Rz group is independently H or C₁-C₄ alkyl, with the proviso that not more than 3 Rz groups may be C₁-C₄ alkyl;

R1 is C₁-C₆ alkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C₁-C₄ alkylthio (optionally substituted with 1, 2 or 3 fluorine atoms), C₁-C₄ alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms), C₃-C₆ cycloalkoxy, C₁-C₄ alkylsulfonyl, cyano, -CO-O(C₁-C₂ alkyl), -O-CO-(C₁-C₂ alkyl) and hydroxy); C₂-C₆ alkenyl (optionally substituted with 1, 2 or 3 halogen atoms); C₃-C₆ cycloalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C₁-C₄ alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; C₄-C₇

cycloalkylalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C₁-C₄ alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; or CH₂Ar₂; and
 Ar₁ and Ar₂ are each independently a phenyl ring or a 5- or 6-membered heteroaryl ring each of which is optionally substituted with 1, 2 or 3 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C₁-C₄ alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C₁-C₄ alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C₁-C₄ alkyl), cyano, -NRR, -CONRR, halo and hydroxy

-336-

and/or with 1 substituent selected from pyridyl, thiophenyl, phenyl, benzyl and phenoxy each of which is optionally ring-substituted with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO₂NRR and SO₂R); and
each R is independently H or C1-C4 alkyl;
or a pharmaceutically acceptable salt thereof.

3. The method of claim 1 or the use of claim 2, wherein said selective norepinephrine reuptake inhibitor is atomoxetine hydrochloride.